

Claims

1. A polynucleotide selected from the group consisting of:
 - (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;
 - (b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;
 - (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
 - (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
 - (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;or the complementary strand of such a polynucleotide.
2. The polynucleotide of claim 1 which is DNA, genomic DNA or RNA.
3. A vector containing the polynucleotide of claim 1 or 2.
4. The vector of claim 3 in which the polynucleotide is operatively linked to expression control sequences allowing expression in prokaryotic and/or eukaryotic host cells.
5. A host cell genetically engineered with the polynucleotide of claim 1 or 2 or the vector of claim 3 or 4.
6. A transgenic non-human animal containing a polynucleotide of claim 1 or 2, a vector of claim 3 or 4 and/or a host cell of claim 5.

7. A process for producing a polypeptide encoded by the polynucleotide of claim 1 or 2 comprising: culturing the host cell of claim 5 and recovering the polypeptide encoded by said polynucleotide.
- 5 8. A process for producing cells capable of expressing at least one of the bitter taste receptor polypeptides comprising genetically engineering cells *in vitro* with the vector of claim 3 or 4, wherein said bitter taste receptor polypeptide(s) is(are) encoded by a polynucleotide of claim 1 or 2.
- 10 9. A polypeptide having the amino acid sequence encoded by a polynucleotide of claim 1 or 2 or obtainable by the process of claim 7.
10. An antibody specifically binding to the polypeptide of claim 9.
- 15 11. A nucleic acid molecule which specifically hybridizes to a polynucleotide of claim 1 or 2.
12. An antagonist/inhibitor against the polypeptide of claim 8 which is an antibody, the extracellular domain of the polypeptide of claim 8 or a fragment thereof or an
20 inhibiting RNA.
13. The antagonist/inhibitor of claim 12, wherein said inhibiting RNA is an antisense construct hybridizing to a polynucleotide of claim 1 or 2, RNAi, siRNA or a ribozyme.
- 25 14. A process for isolating a compound that binds to a polypeptide encoded by a polynucleotide selected from the group consisting of:
 - (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50;
 - 30 (b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49 encoding at least the mature form of the polypeptide;
 - (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more

amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

comprising:

(1) contacting said polypeptide or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide with a compound;

(2) detecting the presence of the compound which binds to said polypeptide; and

(3) determining whether the compound binds said polypeptide.

15. A process for isolating an antagonist of the bitter taste receptor activity of the polypeptide encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NO to the at s 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50;

(b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter taste receptor activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter taste receptor activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter taste receptor activity;

comprising:

(1) contacting said polypeptide or a host cell genetically engineered with said

polynucleotide or with a vector containing said polynucleotide with a potential antagonist;

- (2) determining whether the potential antagonists antagonizes the bitter taste receptor activity of said polypeptide.

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16. The process of claim 15 further comprising the contacting of the polypeptide with an agonist of the respective bitter taste receptor activity.

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17. The process of claim 16 in which said contacting with an agonist is carried out prior, concomitantly or after step (1) of claim 15.

18. The process of claim 16 or 17 in which said polypeptide and said agonist are selected from the group consisting of:

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- (a) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 1 and SEQ ID NO: 2 and the agonist selected from the group consisting of acetylthiourea, N,N-dimethylthioformamide, N,N'-diphenylthiourea, N-ethylthiourea, 2-imidazolidinethione, 4(6)-methyl-2-thiouracil, N-methylthiourea, phenylthiocarbamid, 6-phenyl-2-thiouracil, 6-propyl-2-thiouracil, tetramethylthiourea, thioacetamide, thioacetanilide, 2-thiobarbituric acid, and 2-thiouracil and functional derivatives thereof;

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- (b) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 9 and SEQ ID NO: 10 and the agonist selected from the group consisting of saccharin and acesulfame K and functional derivatives thereof;

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- (c) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 11 and SEQ ID NO: 12 and the agonist selected from the group consisting of saccharin and acesulfame K and functional derivatives thereof;

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- (d) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 13 and SEQ ID NO: 14 and the agonist selected from the group consisting of absinthine and functional derivatives thereof;

- (e) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 15 and SEQ ID NO: 16 and the agonist selected from the group consisting of absinthine and functional derivatives thereof;

- (f) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 19 and SEQ ID NO: 20 and the agonist selected from the group

consisting of absinthine and functional derivatives thereof;

(g) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 37 and SEQ ID NO: 38 and the agonist selected from the group consisting of strychnine, brucine, denatonium benzoate, and absinthine and functional derivatives thereof;

(h) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 41 and SEQ ID NO: 42 and the agonist selected from the group consisting of tyrosine, in particular L-tyrosine, leucine, phenylalanine, histidine, tryptophan and functional derivatives thereof; and

(i) the polypeptide encoded by the polynucleotide of claim 1 or 2 as determined by SEQ ID NO: 43 and SEQ ID NO: 44 and the agonist selected from the group consisting of naphthyl- β -D-glucoside, phenyl- β -D-glucoside, salicin, helicin, arbutin, 2-nitrophenyl- β -D-glucoside, 4-nitrophenyl- β -D-glucoside, methyl- β -D-glucoside, esculin, 4-nitrophenyl- β -D-thioglucoside, 4-nitrophenyl- β -D-mannoside, and amygdalin and functional derivatives thereof.

19. A process for the production of a food or any precursor material or additive employed in the production of foodstuffs comprising the steps of the processes of any of claims 14 to 18 and the subsequent step of admixing the identified compound or antagonist with foodstuffs or any precursor material or additive employed in the production of foodstuffs.

20. A process for the production of a nutraceutical or pharmaceutical composition comprising the steps of the processes of any of claims 14 to 18 and the subsequent step of formulating the compound or antagonist with an active agent in a pharmaceutically acceptable form.

21. A food stuff, including human and animal food stuff, any precursor material or additive employed in the production of foodstuff comprising an antagonist/inhibitor of claim 12 or 13.

22. A nutraceutical or pharmaceutical composition comprising an antagonist/inhibitor of claim 12 or 13 and an active agent and optionally a pharmaceutically acceptable carrier.

23. Use of a polynucleotide of claim 1 or 2, a vector of claim 3 or 4, an antibody of claim 10 or an antagonist/inhibitor of claim 12 or 13 for the manufacture of a medicament for the treatment of an abnormally increased or decreased sensitivity towards a bitter substance.

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